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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/035,368	10/26/2001	James P. Hoeffler	IVGN 274.2	2504

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EXAMINER	
COOK, LISA V	
ART UNIT	**PAPER NUMBER**
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/035,368	HOEFFLER ET AL.	
	Examiner	Art Unit	
	Lisa V. Cook	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18,71-82,84 and 88-92* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18,71-82,84 and 88-92* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/19/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. Applicants' response to the Office Action mailed 5/18/07 is acknowledged (Paper filed 11/19/07). In the amendment filed therein claim 18 was modified. Claims 1-17, 19-70, 83, and 85-87 have been canceled. New claims 88-92 have been added. Currently, claims 18, 71-82, 84 and 88-92 are pending and under consideration.

2. Rejections and/or objections of record not reiterated below have been withdrawn.

NEW GROUNDS OF REJECTIONS NECESSITATED BY AMENDMENT

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

I. Claims 18, 71, and 88-92 are rejected under 35 U.S.C. 103(a) as being obvious over Unla et al. (Electrophoresis, 1997, 18, pages 2071-2077) in view of Bernard Blanc (Bulletin de la Societe de Chimie Biologique, 1959, Vol.41, 891-899, English Abstract) and further in view of Chu et al. (ACS Symposium Series, 1997, 657 (Immunochemical Technology for Environmental Applications, pages 170-184), Abstract Only.

Unla et al. teach assay procedures to detect protein differences between two samples. The protein differences between two samples are evaluated in a modified 2-DE (two dimensional polyacrylamide gel electrophoresis) technique called difference gel electrophoresis (DIGE). In particular, two protein samples are labeled with two cyanine dyes. This allows for the simultaneous measurement of both samples on the same gel. Differences in the two samples due to differences in gene expression or protein modification can be identified quickly. See page 2071, 2nd column .

In one embodiment *E. coli* transformed with the chimeric protein GAL4VP16 were induced for 15 min with IPTG. Extracts (Applicant's cell extracts) were labeled with either Cy3 or Cy5 and compared. See figure 4 on page 2076, for example.

Unla et al. are silent with respect to antibody utility in their two dimensional electrophoresis procedures.

However, Bernard Blanc teaches that the technique of 2-dimensional immunoelectrophoresis involves two consecutive electrophoresis at right angles followed by diffusion of specific antibodies in a gelatin medium. This process make it possible to better separate antigen-antibody precipitation arcs and thus allows for an easier differentiation of the corresponding constituents.

The method was evaluated in normal human serum and led to better differentiation in the zones of α2-, β2-, and γ-globulins. Moreover, the procedure offers the advantage of allowing the combination of several other interesting techniques and makes possible a change of conditions between the first and the second electrophoresis. It, thus, becomes a method of interest in the study of complex protein mixtures, such as different biological fluids. See abstract.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use antibodies in electrophoresis procedures as taught by Bernard Blanc in the 2D electrophoresis method of Unla et al. because Bernard Blanc taught that 2D electrophoresis including antibodies makes it possible to better separate antigen-antibody precipitation arcs and thus allows for an easier differentiation of the corresponding constituents. The procedure offers the advantage of allowing the combination of several other interesting techniques and makes possible a change of conditions between the first and the second electrophoresis. See abstract to Blanc.

One of ordinary skill in the art would have been motivated to employ the 2D antibody procedure taught by Blanc because Blanc taught that this was a method of interest in the study of complex protein mixtures, such as different biological fluids. See abstract.

Unla et al. in view of Blanc differ from the instant invention in not specifically teaching the use of an antibody array.

However, antibody arrays were taught in the prior art by Chu et al. Chu et al. teach that microarray based assays (antibody spot immunoarrays) are potentially capable of determining the amounts of hundreds of different analytes in a small sample. Arrays allow for the measurement of many different analytes simultaneously. See Chu et al. abstract.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use antibody arrays as taught by Chu et al. in method of Unla et al. in view of Blanc because Chu et al. taught that microarray based assays (antibody spot immunoarrays) are potentially capable of determining the amounts of hundreds of different analytes in a small sample. Arrays allow for the measurement of many different analytes simultaneously. See Chu et al. abstract.

II. Claims 72-75, 77 and 80-82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Unla et al. (Electrophoresis, 1997, 18, pages 2071-2077) in view of Bernard Blanc (Bulletin de la Societe de Chimie Biologique, 1959, Vol.41, 891-899, English Abstract) and further in view of Chu et al. (ACS Symposium Series, 1997, 657 (Immunochemical Technology for Environmental Applications, pages 170-184), Abstract Only as applied to claims 18, 71, and 88-92 above, and further in view of Ekins et al. (Clin Chem. 37/11, 1955-1967, 1991).

Please Unla et al. in view of Bernard Blanc and further in view of Chu et al. as set forth above.

Unla et al. in view of Bernard Blanc and further in view of Chu et al. differ from the instant invention in not specifically teaching multiple antigens and antibody preparations.

However, Ekins et al. teach method to detect proteins via multianalyte microspot immunoassays. An array of antibodies (device comprising multiple immobilized agents for protein detection such as antibodies) is exposed to proteins to monitor the expression and properties of a large number of proteins. See abstract and figures 4 and 5.

The detection procedure can be evaluated with a radioactive isotopes (i.e. I^{125}), an enzyme, chemiluminescent label, or fluorescence label. See page 1960. In one embodiment dual microspot assay devices are compared. See page 1961 figure 8 for example. The microarrays taught by Ekins can measure tens, hundreds, or thousands of analytes. Thus the array may comprising 106 Ab (antibody) micro-spots each directed against a different analyte See abstract.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the protein patterning procedures as taught by Unla et al. in view of Bernard Blanc and further in view of Chu et al. with multiple antigens and antibodies as exemplified by Ekins et al. because Ekins et al. taught that antibody arrays can be configured to measure tens, hundreds, or thousands of analytes. See abstract.

Absent evidence to the contrary the adjustment of the prior art to employ multiple antigens and antibodies is deemed routine. It has been held that the provision of adjustability, where need, involves only routine skill in the art. *In re Stevens*, 101 USPQ 284 (CCPA 1954).

One of ordinary skill in the art would have been motivated to utilize multiple antigens and antibodies in order to generate more data sets for analysis.

III. Claims 76, 78-79 and 84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Unla et al. (Electrophoresis, 1997, 18, pages 2071-2077) in view of Bernard Blanc (Bulletin de la Societe de Chimie Biologique, 1959, Vol.41, 891-899, English Abstract) and further in view of Chu et al. (ACS Symposium Series, 1997, 657 (Immunochemical Technology for Environmental Applications, pages 170-184), Abstract Only as applied to claims 18, 71, and 88-92 above, and further in view of James F. Cupo (Journal of Chromatography, 569, 1991, 389-40).

Please Unla et al. in view of Bernard Blanc and further in view of Chu et al. as set forth above.

Unla et al. in view of Bernard Blanc and further in view of Chu et al. differ from instant invention in not teaching protein expression pattern evaluation in cancer diseases or virus cell lines (like T cells).

However, Cupo teaches a two-dimensional polyacrylamide gel electrophoresis procedure to measure matrix proteins. The proteins are tissue-type specific and can reflect changes in the state of differentiation of a cell. The method can further distinguish between a diseased cell and a normal cell. The disease states include various cancers, autoimmune disease, and adenoviral infection. See abstract.

The method is quick and efficient employing the appropriate antibodies to the protein of interest. Page 403, 1st paragraph. Protein patterning in T lymphocytes (T cells) is outlined on page 400. The method is used to detect early stages of viral infection because a virus must replicate cellular components associated with the nuclear matrix. Such changes are evident in protein patterning analysis. See page 403 – 4.3.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use protein patterning procedures to evaluate cancer diseases or virus cell lines (like T cells) and further allowing for cellular replication distinctions (differential development) via polyacrylamide as taught by Cupo in the protein procedure of Unla et al. in view of Bernard Blanc and further in view of Chu et al. because Cupo taught that two-dimensional gels can determine tissue-type specific differences in nuclear matrix proteins and the differences between normal and carcinogenic cells. See page 402 - 4.2 Further these proteins play an important role in cells.

Utilization of the proteins can lead to the development of diagnostic agents to detect various diseased conditions of the cell and organism (including cancer and viruses). Cupo page 404.

Response to Arguments

4. Applicant's argument's filed 11/19/07 against the previously cited art is MOOT because new claims and new rejections have been presented in the instant office action.

In particular, applicant contends that Brott et al. taught cell lystate contact with an antibody in solution, not on a solid support to form immunoprecipitates, not to generate a binding pattern with two different labeling dyes. While Piehler et al. is not directed to microarrays. Brott et al. in view of Piehler et al. have been replaced with Unla et al. in view of Bernard Blanc and further in view of Chu et al. to make the claimed invention obvious.

With respect to the reference of Ekins et al., Applicant argues that the reference is not enabled because Ekins et al. present s theoretical analysis of antibody-antigen binding without experimental support. This argument was carefully considered but not found persuasive because a reference is not limited to its working examples, but must be evaluated for what it teaches those of ordinary skill in the art. *In re Boe*, 355 F.2d 961, 148 USPQ 507 (CCPA 1966). *In re Chapman*, 357 F.2d 418, 148 USPQ 711 (CCPA 1966). Ekins et al. were recited to merely teach the use of multiple antigen-antibody combinations in microarrays. The microarrays taught by Ekins can measure tens, hundreds, or thousands of analytes. Thus the array may comprising 106 Ab (antibody) micro-spots each directed against a different analyte See abstract. This teaching makes the claimed microarray configurations obvious.

Applicant contends that Cupo does not overcome the deficiencies of Brott et al. in view of Piehler et al. Accordingly, Cupo has been combined with Unla et al. in view of Bernard Blanc and further in view of Chu et al. to make the claimed invention obvious

5. For reasons aforementioned, no claims are allowed.

Remarks

6. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

A. Fields et al. (U.S. Patent #5,283,173) disclosed systems to measure protein-protein interactions.

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Papers related to this application may be submitted to Group 1600 by facsimile transmission. The Group 1641 – Central Fax number is (571) 273-8300, which is able to receive transmissions 24 hours/day, 7 days/week.

In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to Group TC 1600 whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see httpr//pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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